

WHAT IS CLAIMED IS:

1. An isolated immunogen comprising an HIV envelope protein bound to a ligand, which ligand upregulates at least one of the CD4 binding site and the CCR5 binding site on said protein.

2. The immunogen according to claim 1 when said HIV protein is gp120, uncleaved gp140 or gp120 noncovalently bound to gp41.

3. The immunogen according to claim 1 wherein said ligand is an antibody, or Fab<sub>2</sub> or Fab fragment thereof.

4. The immunogen according to claim 2 wherein said ligand binds to a CCR5 binding site on gp120 and upregulates a CD4 binding site on gp120.

4 ~~5~~. The immunogen according to claim <sup>3</sup>~~4~~ wherein said ligand is an antibody, or Fab<sub>2</sub> or Fab fragment thereof.

5 ~~6~~. The immunogen according to claim <sup>3</sup>~~4~~ wherein said ligand is monoclonal antibody (mab) 17b, or Fab<sub>2</sub> or Fab fragment thereof, or mimic thereof.

Sub C7  
7. The immunogen according to claim 1 wherein said ligand upregulates a CCR5 and a CD4 binding site on gp120.

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7.8. The immunogen according to claim 7 wherein said ligand is an antibody, or Fab<sub>2</sub> or Fab fragment thereof.

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8.8. The immunogen according to claim 7 wherein said ligand binds to a site on gp120 to which mab A32 binds.

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9 10. The immunogen according to claim 8 wherein said ligand is mab A32, or Fab<sub>2</sub> or Fab fragment thereof, or mimic thereof.

11. The immunogen according to claim 1 wherein said protein and said ligand are crosslinked.

Sub C8  
12. The immunogen according to claim 1 wherein said protein is in soluble form.

13. The immunogen according to claim 1 wherein said protein is associated with a cell vesicle or liposome.

14. The immunogen according to claim 1 wherein said protein is gp120 noncovalently bound to gp41.

15. The immunogen according to claim 14 wherein gp120, gp41 and said ligand are crosslinked.

16. The immunogen according to claim 14 wherein said immunogen further comprises an HR-2 peptide bound to said protein.

<sup>13</sup> 17. The immunogen according to claim <sup>1</sup> 16 wherein gp120, gp41, said ligand and said HR-2 peptide are crosslinked.

18. A composition comprising at least one immunogen according to claim 1 and a carrier.

19. A method of inducing the production of neutralizing antibodies to HIV in a mammal comprising administering to said mammal an amount of said immunogen according to claim 1 sufficient to effect said induction.

20. A method of screening a compound for its ability to upregulate the CD4 binding site on gp120 comprising contacting said compound with gp120 and mab 17b, or Fab<sub>2</sub> or Fab fragment thereof, or mimic thereof,

and determining whether said compound competes with mab 17b, or fragment or mimetic thereof, for binding to the CCR5 binding site on said gp120, wherein a compound that competes with mab 17b, or fragment or mimetic thereof, is a compound that potentially upregulates the CD4 binding site on gp120.

21. The method according to claim 20 wherein mab 17b, or fragment or mimetic thereof, bears a detectable label.

22. The method according to claim 20 wherein gp120 is bound to a solid support.

23. The method according to claim 22 wherein said solid support is BIACORE chip.

24. A method of screening a compound for its ability to upregulate the CD4 and CCR5 binding sites on gp120 comprising contacting said compound with gp120 and mab A32, or Fab<sub>2</sub> or Fab fragment thereof, or mimic thereof, and determining whether said compound competes with mab A32, or fragment or mimetic thereof, for binding to gp120, wherein a compound that competes with mab A32, or fragment or mimetic thereof is a compound that potentially upregulates the CD4 and CCR5 binding sites on gp120.

25. The method according to claim 24 wherein mab A32, or fragment or mimetic thereof, bears a detectable label.

26. The method according to claim 24 wherein gp120 is bound to a solid support.

27. The method according to claim 26 wherein said solid support is BIACORE chip.

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